Paper No. 37

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte TINYU LI and YAN WANG

Appeal No. 2004-0275
Application No. 09/318,186

ON BRIEF[1]

Before WINTERS, WILLIAM F. SMITH, and MILLS, Administrative Patent Judges.

MILLS, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on the appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 60-65, 67-69, 71, 74, 77, and 80[2], which are all the pending claims in the application.

[1] Appellants waived their request for oral hearing, therefore we consider this appeal on Brief.

[2] The examiner's Answer refers to a claims 72, 73, 78 and 79 in error, as these claims were cancelled in Paper No. 31. The above stated claims are the only claims at issue in this appeal.

Claim 60 is illustrative of the claims on appeal and reads as follows:

60. A method for screening chiral selectors from a parallel library comprising:

(a) forming a parallel library by individually synthesizing chiral selectors onto a polymeric synthesis resin;

(b) incubating each individual chiral selector, attached on the polymeric resin, with an analyte having a mixture of a R-enantiomer and a S-enantiomer:

(c) analyzing the resultant of step (b) to identify which chiral selector selectively adsorbed one of the R-enantiomer and the S-enantiomer;

(d) attaching the identified chiral selector onto a support; and

(e) resolving the analyte of step (b) into the R-enantiomer and the S-enantiomer with the attached chiral selector on the support.

The references relied upon by the examiner are:

Lam et al. (Lam) 5,858,670 Jan. 12, 1999

Welch, et al. (Welch), "Microscale Synthesis and Screening of Chiral Stationary Phases," Enantiomer, Vol. 3, pp. 471-476 (1998).

Liu, et al. (Liu), "Polymer- versus Silica-Based Separation Media: Elimination of Nonspecific Interactions in the Chiral Recognition Process through Functional Polymer Design," Anal. Chem., Vol. 69, pp. 61-65 (1997).

Weingarten, et al. (Weingarten), "Enantioselective Resolving Resins from a Combinatorial Library. Kinetic Resolution of Cyclic Amino Acid Derivatives," J. Am. Chem. Soc., Vol. 120, pp. 9112-9113 (1988).

Pirkle, et al. (Pirkle), "A Chiral Stationary Phase Which Affords Unusually High Levels of Enantioselectivity," Chirality, Vol. 3, pp. 183-187 (1991).

Grounds of Rejection

Claims 60-65, 67, 69, 71, 74 and 80 stand rejected under 35 U.S.C. § 103(a) for obviousness over Welch in view of Liu and further in view of Weingarten.

Claims 60 and 77 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Welch, Liu, and Weingarten, in view of Lam.

Claims 60-65, 67-69, 71 and 74 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Welch, Liu, and Weingarten in view of Pirkle.

We affirm these rejections.

Claim Grouping

According to appellants, the claims stand or fall together. Appeal Brief, page 5. Since the individual claims are not argued, we decide this appeal with respect to the prior art rejection on the basis of claim 60. 37 CRF § 1.192(c)(7) (1998). In re McDaniel, 293 F.3d 1379, 63 USPQ2d 1462, 1466 (Fed. Cir. 2002).

DISCUSSION

In reaching our decision in this appeal, we have given consideration to appellants' specification and claims, to the applied references, and to the respective positions articulated by appellants and the examiner. As a consequence of our review, we make the determinations that follow.

35 U.S.C. § 103(a)

Claims 60-65, 67, 69, 71, 74 and 80[3] stand rejected under 35 U.S.C. §103(a) for obviousness over Welch in view of Liu and further in view of Weingarten. In addition, claims 60 and 77 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Welch, Liu, and Weingarten, in view of Lam. Furthermore, claims 60-65, 67-69, 71 and 74 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Welch, Liu, and Weingarten in view of Pirkle. Claim 60 is selected as the representative claim for each rejection.

In rejecting claims under 35 U.S.C. § 103(a), the examiner bears the initial burden of presenting a prima facie case of obviousness. See In re Rijckaert, 9 F.3d 1531, 1532, 28 USPQ2d 1955, 1956 (Fed. Cir. 1993). A prima facie case of obviousness is established when the teachings from the prior art itself would appear to have suggested the claimed subject matter to a person of ordinary skill in the art. In re Bell, 991 F.2d 781, 783, 26 USPQ2d 1529, 1531 (Fed. Cir. 1993).

Claim 60 is directed to a "method for screening chiral selectors" and includes steps of synthesizing chiral selectors onto a polymer resin, incubating the chiral selector with an analyte, analyzing the selectors to identify which ones selectively adsorbed which enantiomers, attaching the identified selectors onto a support, and resolving the analyte mixture with the attached chiral selector. It is

[3] As noted in the Answer, page 2, claim 80, added in an amendment after final rejection is rejected on the same basis as claim 60.

the examiner's position that the instant claims are obvious in light of Welch, in view of Liu, and further in view of Weingarten.

Welch teaches a method for rapid screening of libraries of candidate chiral selectors using a parallel library. Answer, page 8. Microscale synthesis and screening is performed by Welch to evaluate the enantioselectivity of the candidate chiral stationary phases. Id. Welch uses libraries synthesized on silica; therefore the reference lacks the teaching of using the polymeric synthesis resins set forth in the instant claim. Id. Liu teaches that silica has disadvantages such as nonspecific interactions and polymer beads have desirable characteristics. Answer, page 10.

According to the examiner (Answer, pages 6-7):

> [I]t would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to make the library of chiral selectors taught by Welch et al on amino functionalized polystyrene as taught by Weingarten et al. A person of ordinary skill in the art would have been motivated to do so based on the teachings of Liu et al that using a polymer support avoids the disadvantages of silica and allows for a potential enhancement of enantioselectivity. Weingarten et al also teach that such polymer supported materials can be easily synthesized and screened. Moreover, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to further use the identified selectors in additional separations, as taught by Welsh [sic] et al.

We agree that the examiner has presented sufficient evidence to support a prima facie case of obviousness. In particular, Welch describes a parallel library system for use in the microscale synthesis and screening of chiral molecule stationary phases which is very similar to the claimed invention.

However, Welch synthesizes its chiral stationary phase on silica, as opposed to a polymeric resin, as claimed. Liu recites the advantages of using a polymeric stationary phase in place of a silica phase in chiral molecule resolution. Although Liu uses the polymer stationary phase at a later step in a chiral separation process than in claim 60 steps (a)-(c), the disadvantages of silica, namely nonspecific interactions caused by the presence of residual silanol groups, and advantages associated with the use of a polymeric resin, would have been recognized by one of ordinary skill in the art as also applicable to a step of screening for chiral selectors as well as a step of using the selectors to separate a mixture.

Steps (d) and (e) of claim 60 are directed toward using the library of chiral selectors synthesized in steps (a)-(c) to separate a mixture of enantiomers. This use, although not specifically described in Welch, is suggested at page 471, column one, which states that the selective stationary phases are useful for large scale preparative enantioseparation. Weingarten specifically uses a selective library to resolve a solution, separating a racemic mixture. Thus, in our view, Weingarten in combination with Welch and Liu, would have reasonably suggested the claimed chiral separation method to one of ordinary skill in the art.

Where the prior art, as here, gives reason or motivation to make the claimed invention, the burden then falls on appellants to rebut that prima facie case. Such rebuttal or argument can consist of any other argument or

presentation of evidence that is pertinent. In re Dillon, 919 F.2d 688, 692-93, 16 USPQ2d 1897, 1901 (Fed. Cir. 1990) (en banc), cert. denied, 500 U.S. 904 (1991).

Appellants argue that the instant claims are not obvious under 35 U.S.C. §103 in view of the cited references. Brief, page 12. Appellants argue that, "one of ordinary skill in the art would not look to bits and pieces of the secondary references in that manner suggested if the references are considered as a whole." Brief, page 6. Appellants point out that Welch does not describe synthesizing chiral selectors on a polymeric synthesis resin, Liu does not describe synthesizing chiral selectors on a resin, and Weingarten fails to disclose forming a parallel library. Brief, pages 5-9.

These attempts to rebut the examiner's prima facie case of obviousness are unpersuasive. Obviousness can be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. In re Fine, 837 F.2d 1071, 1074, 5 USPQ2d 1596, 1598 (Fed. Cir. 1988), In re Jones, 958 F.2d 347, 350, 21 USPQ2d 1941, 1943 (Fed. Cir. 1992).

We agree with the examiner that the prior art references provide the necessary reason, suggestion or motivation to make the claimed invention and we are not persuaded by appellants' arguments to the contrary. Appellants

cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. In re Keller, 642 F.2d 413, 425, 208 USPQ 871, 881 (CCPA 1981); In re Merck & Co., Inc., 800 F.2d 1091, 1097, 231 USPQ 375, 380 (Fed. Cir. 1986).

More particularly, appellants argue that Welch does not describe "synthesizing chiral selectors onto a polymeric synthesis resin. However, the examiner explains that Liu provides the motivation to combine the polymer base with Welch and Weingarten by describing the advantages of the use of a polymer resin over the silica base in preparing chiral molecule selectors. Answer, pages 6-7.

Additionally, appellants argue that Welch does not describe using the polymeric resins set forth in claim 60, (i.e., does not describe steps (d) and (e)), namely the use of a screening library for the resolution of a racemic mixture. The examiner acknowledges Welch lacks the specific teaching of steps (d) and (e), but notes that Welch states in both the introduction and conclusion that the purpose of screening the chiral stationary phases (CSPs) is to identify CSPs useful for large scale preparative enantioseparation. Answer, page 5. In addition, Liu recites steps for synthesizing the selector on a base, and Weingarten uses a selector library to resolve a mixture. Thus, appellants' arguments are unpersuasive when viewed in light of the combination of references.

According to appellants, although Liu states that silica has disadvantages, and describes the use of a polymer base, Liu does not offer strong motivation to combine the references because Liu does not prepare chiral selectors onto polymeric synthesis resin for subsequent use in a step that would correspond to the synthesis step of the present invention. Brief, page 7. In addition, appellants argue that Liu describes chiral separation according to step (d), a downstream step of the claimed process, and it is inappropriate to use Liu as a teaching of claim 60, synthesis step (a), as Liu fails to disclose or suggest a process of individually synthesizing a chiral selector onto a polymeric synthesis resin. Id., pages 7-8. Thus, according to appellants, one would not be motivated to combine the references.

However, Liu is used by the examiner as evidence to suggest that a polymer base has advantages over a silica base in chiral compound selection. Answer, page 6. In our view, Liu provides a strong motivation to combine with Welch and Weingarten to establish obviousness because it emphasizes advantages of a polymer base over a silica base in chiral molecule selection. The strongest rationale for combining references is a recognition, expressly or impliedly in the prior art or drawn from a convincing line of reasoning based on established scientific principles or legal precedent, that some advantage or expected beneficial result would have been produced by their combination In re Sernaker, 702 F.2d 989, 994-995, 217 USPQ 1, 5-6 (Fed. Cir. 1983). Liu

teaches that silica has disadvantages, such as allowing for nonspecific interactions between polar silanol groups and analyte enantiomers. Liu then goes on to state that polymer bases overcome the disadvantages of a silica base, thereby increasing the yield of a resolution. Since Liu discusses the advantages of using a polymer base over a silica base for chiral molecule selection, it provides a strong reason, suggestion or motivation to substitute a polymer base for a silica base in chiral molecule resolution and selection.

Furthermore, appellants argue that Weingarten discloses a method of preparing chiral resolution resins using a different procedure than the procedure claimed in the invention. Brief, page 9.

Appellants argue that Weingarten is directed to a different type of procedure altogether, and that one of ordinary skill in the art would not associate it with Liu or Welch. Id. Appellants argue that the method of Weingarten is a pool/split procedure, where polymer beads are pooled and re-divided during synthesis. Id. Appellants state that the claims in the present invention are directed to a parallel library, and thus argue that the Weingarten reference has no connection to the present invention. Brief, pages 9-12.

However, Weingarten is not cited by the examiner for the method used to prepare the library. Weingarten is cited for its teaching of a library of chiral selectors immobilized on polymer beads. Answer, page 6. It is of no consequence that the procedure used in Weingarten is a split/pool procedure

and not a parallel library, as Welch discloses and is relied on for its use of a parallel library.

In view of above, the rejections of claims 60-65, 67, 69, 71, 74 and 80 over Welch, Liu and Weingarten are affirmed. The rejections of claims 60 and 77 under 35 U.S.C. § 103(a) as being unpatentable over Welch, Liu, and Weingarten, in view of Lam, and claims 60-65, 67-69, 71 and 74 under 35 U.S.C. § 103(a) as being unpatentable over Welch, Liu, and Weingarten in view of Pirkle, also fall with claim 60 based upon the primary combination of references.

CONCLUSION

The rejection of claims 60-65, 67, 69, 71, 74 and 80 under 35 U.S.C. § 103(a) for obviousness over Welch in view of Liu and further in view of Weingarten is affirmed.

The rejections of claims 60 and 77 under 35 U.S.C. § 103(a) as being unpatentable over Welch, Liu, and Weingarten, in view of Lam, and claims 60-65, 67-69, 71 and 74 under 35 U.S.C. § 103(a) as being unpatentable over Welch, Liu, and Weingarten in view of Pirkle, also fall with claim 60 based upon the primary combination of references and are affirmed.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 CFR § 1.136(a).

AFFIRMED

SHERMAN D. WINTERS Administrative Patent Judge	))))) BOARD OF PATENT
WILLIAM F. SMITH Administrative Patent Judge	)) APPEALS AND))) INTERFERENCES
DEMETRA J. MILLS Administrative Patent Judge	))

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